

REMARKS

Entry and consideration of this amendment, along with the accompanying Request for Continued Examination, are respectfully requested.

I. Status of the Claims

Claims 1-3, 6-19, 23, 24, 26, and 27 are pending.

Claims 4, 5, 20-22, and 25 are canceled without prejudice.

II. Amendments to the Claims

Claim 1 has been amended to reflect a conjugate that consists essentially of a peptide that is either biphalin or DPDPE covalently linked to one or more polymer chains that are either polyethylene glycol or copolymers of ethylene glycol and propylene glycol, where the one or more polymer chains optionally possesses an agent covalently attached thereto, where the agent is selected from a neuroactive agent, doxorubicin, an imaging agent, and a diagnostic agent. Support for this amendment is found in pending claims 17, 19, and throughout the specification as originally filed. Support for one or more polymer chains covalently attached to the active agent is found in the specification at page 9, paragraph [0038] to paragraph [0042].

Amendments to the remaining claims are to conform to the language of newly amended claim 1, and to provide proper antecedent basis for the terms recited therein.

No new matter has been added to the claims by virtue of the amendments presented herein.

Although the present communication may include alterations to the claims and characterizations of claim scope or cited art, the Applicant is in no way conceding that previously pending claims are not patentable over the cited references. Applicant reserves the right to pursue at a later date any previously pending or other broader or narrower claims that capture subject matter supported by the present disclosure,

including subject matter that may have been disclaimed herein or by any prior prosecution directed to the subject matter described in the present disclosure.

III. Prior Art Rejections: Rejections Under 35 U.S.C. §103

A. GROUND OF REJECTION.

The Examiner has maintained his rejection of claims 1-3, 5-19, 21, 23, 26, and 27 under 35 U.S.C. §103(a) as unpatentable over Delgado, et al., and Wu, et al.

Specifically, the Examiner has maintained his position, that, based upon the teachings of Delgado and Wu, it would have been obvious at the time of the invention to arrive at a peptide that is either biphalin or DPDPE, covalently attached to a water soluble polymer such as those recited in claim 1, to provide a hydrophilic conjugate capable of transport across the blood brain barrier when administered to the blood circulation.

This rejection is respectfully traversed for the reasons which follow, and those already of record.

B. THE INVENTION

The Examiner is reminded that the claims are not only directed to particular peptide-polymer conjugates, but also to conjugates capable *per se* of transport across the blood brain barrier – absent a transport vector of the type required by Wu, and further absent lipophilic moieties believed to facilitate transport of such peptides across the blood-brain barrier (BBB).

C. CITED ART

Delgado, et al. and Wu et al. have been extensively characterized in Applicant's previous Amendments, and such characterizations are not repeated here.

D. ARGUMENT

In determining whether a claimed invention is obvious, the following tenants must be adhered to:

- i. The claimed invention must be considered as a whole;

- ii. The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination or modification; and
- iii. The references must be viewed without the benefit of hindsight afforded by the claimed invention or accompanying specification.

A prior art references must be considered in its entirety, i.e., as a whole, *including portions that would lead away from the claimed invention. W.L. Gore & Associates, Inc. v. Garlock, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983).*

The Cited References Fail to Suggest the Claimed Subject Matter, and Fail to Provide Motivation to Modify to Arrive at the Claimed Subject Matter

"The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to solved as a whole would have suggested to those of ordinary skill in the art." *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ 1313, 1317 (Fed. Cir. 2000), *In re Lee*, 277 F.3d 1338, 1342-44, 61 USPQ2d 1430, 1433-34.

The claims under consideration are directed to a hydrophilic polymer-peptide conjugate consisting essentially of a peptide that is either biphalin or [D-Pen², D-Pen⁵] enkephalin (DPDPE) covalently linked to one or more polyethylene glycol or ethylene glycol-propylene glycol co-polymer chains having a molecular weight from about 2,000 to about 100,000 daltons, where the conjugate, when administered into the blood circulation of a mammal, is capable of transport across the blood brain barrier. Additional optional features of the polymer can be found in claim 1.

The conjugates of the claimed invention are absent a lipophilic moiety or any sort of transport vector, both of which were thought at the time of the invention to be critical to the transport of peptides such as DPDPE or biphalin across the BBB.

In view of the above, it is submitted that the Examiner is improperly extending the teachings of the general PEGylation reference of Delgado to the instant claims, and failing to acknowledge the state of the art as a whole at the time of the invention, particularly with respect to neuropeptides such as those claimed, and their inability to cross the BBB. For instance, Wu actually teaches away from the Applicant's claims,

since Wu teaches that in order for a neurotrophic factor such as BDNF to cross the blood brain barrier, it must not only be modified to possess optimized plasma pharmacokinetics (e.g., via covalent attachment to PEG), but *must* also be conjugated to a transport vector such as OX26 mAB. The conjugates of the Applicant's claims are clearly absent such a feature. To modify the teachings of Wu to arrive at the claimed invention, one would not only have to change the described neurotrophic factor to a small neuropeptide such as biphalin or DPDPE, but would further have to eliminate a feature of Wu stated to be critical for transport of BDNF across the BBB - i.e., the transport vector. Such a modification would, when viewed without the benefit of hindsight provided by the Applicant's application, render the conjugate of Wu inoperable for transport across the BBB. The Examiner is reminded that: "If a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

Thus, the combination of references relied upon by the Examiner fails to provide any motivation whatsoever to modify the teachings therein to arrive at a conjugate of the type embodied in the Applicant's claims.

In view of the above, it is submitted that nowhere does the art relied upon by the Examiner suggest or provide the slightest motivation to covalently attach a polymer of the type claimed to either DPDPE or biphalin, to provide a conjugate capable of transport across the blood brain barrier.

In sum, it is submitted that the pending claims comply with the standards of 35 U.S.C. §103. Withdrawal of the rejection of the claims under 35 U.S.C. §103 is therefore respectfully requested.

IV. Information Disclosure Statement

The Applicant has previously informed the Examiner of the prosecution of co-pending Application No. 10/354,683 (the '683 application). In the event that information of record in the '683 application may be considered by the Examiner to be relevant to the patentability of the instant claims, copies of Office Actions issued by the Examiner in

such case, as well as the Applicant's reply thereto, are provided herein for the Examiner's consideration.

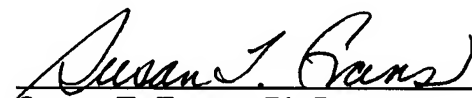
V. Conclusion

In view of the foregoing, the Applicant submits that all of the claims pending in the application patentably define over the cited art. A Notice of Allowance is therefore respectfully requested.

If a telephone conference would expedite the prosecution of the subject application, the Examiner is requested to call the undersigned at (650) 838-4406.

Respectfully submitted,
Perkins Coie LLP

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